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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,971	02/16/2005	Salvatore Avolio	ITT0039YP	1846

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EXAMINER	
RAO, DEEPAK R	
ART UNIT	PAPER NUMBER
1624	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/23/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,971	AVOLIO ET AL.	
	Examiner	Art Unit	
	Deepak Rao	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-9,11,13 and 14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-9,11,13 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20060330*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 3-9, 11 and 13-14 are pending in this application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating an illness due to hepatitis C virus, does not reasonably provide enablement for a method of inhibiting hepatitis C virus polymerase generally; or a method of preventing an illness due to hepatitis C virus. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed. The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations.

The instant claims are drawn to 'a method of inhibiting hepatitis C virus polymerase' and 'a method of treating or **preventing** an illness due to hepatitis C virus'. First, the instant claim covers diseases or disorders caused by 'hepatitis C virus', those that are known to exist and those that may be discovered in the future, for which there is no enablement provided. The test procedure provided in the specification page 20 does not provide any data correlating the activity of the instant compounds with the instantly claimed methods generally and none of the compounds have been tested for the activity to cover the effectiveness for the method of inhibiting hepatitis C virus polymerase generally or a method of treating or preventing all types of illnesses due to hepatitis C virus. Further, there is no reasonable basis for assuming that the myriad of compounds embraced by the claims will all share the same physiological properties since they are so structurally dissimilar as to be chemically non-equivalent and there is no basis in the prior art for assuming the same. Note *In re Surrey*, 151 USPQ 724 regarding sufficiency of disclosure for a Markush group. Also see MPEP § 2164.03 for enablement requirements in cases directed to structure-specific arts such as the pharmaceutical art. Receptor activity is generally unpredictable and highly structure specific area. It is inconceivable as to how the claimed compounds can treat all types of diseases caused due to herpes viral infections.

Furthermore, the scope of the method claim 14, is not adequately enabled solely based on hepatitis C virus inhibitory activity provided in the specification. The instant claim is drawn to 'a method of .... **preventing** an illness due to hepatitis C virus', and therefore, the instant claim language embraces disorders not only for the treatment, but for "prevention" which is not remotely enabled. The instant compounds are disclosed have hepatitis C virus inhibitory activity and it is recited that the instant compounds are useful in the "prevention" of all types of illnesses

due to hepatitis C virus, for which applicants provide no competent evidence. "To prevent" actually means *to anticipate* or *counter in advance, to keep from happening etc.* (as per Websters II Dictionary) and therefore it is not understood how one skilled in the art can reasonably establish the basis and the type of subject to which the instant compounds can be administered in order to have the "prevention" effect. A recent article by Camma et al., provides that 'many unanswered questions remain regarding hepatitis C virus'. Thus, it is inconceivable as to how the claimed compounds can not only treat but also "prevent" a myriad of diseases with different etiologies. Further, applicants have neither disclosed nor provided any evidence that the a method of preventing infection due to hepatitis C virus exists or known. There is no evidence of record, which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disease(s) or disorder(s) claimed herein.

(Only a few of the references pertinent to the claims are discussed here to make the point of an insufficient disclosure, it does not definitely mean that the claims meet the enablement requirements with respect to other members of herpes viruses).

1) The nature of the invention: Therapeutic use of the compounds in method of inhibiting hepatitis C virus, and method of treating or preventing hepatitis C virus.

2) The state of the prior art: There are no known compounds of similar structure which have been demonstrated to treat and/or prevent all types of illnesses due to hepatitis C virus.

3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously

varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

4) The amount of direction or guidance present and 5) the presence or absence of working examples: The specification provides tests to determine the activity of the compounds in relation to inhibition of HCV RdRp.

6) The breadth of the claims: The instant claims embrace method of inhibiting hepatitis C virus polymerase, and method of treating or preventing hepatitis C virus.

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the use of the invention. In view of the breadth of the claim, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-9, 11, 13 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gardelli et al., WO 02/006246 (International filing date July 11, 2001). The reference teaches 2-aryldihydroxypyrimidine-4-carboxylic acid compounds useful as inhibitors of hepatitis C virus polymerase, see formula (I) in page 3 and the species of the Examples. The reference discloses that the compounds exist in equilibrium with the corresponding tautomeric form of structural formula (IA) as disclosed in page 3. The instant claims differ from the reference compounds by having the substituent attached to the ring nitrogen atom, R^1 as an alkyl group, e.g., a methyl (CH_3), as compared to the reference compounds of formula (IA), which have H in the analogous position. Therefore, the instantly claimed compounds differ from the reference compounds by having H vs. CH_3 group and the structural similarity of compounds differing by a methyl in place of the hydrogen (i.e., H vs. Methyl) is well established. It would have been obvious to one having ordinary skill in the art at the time of the invention to modify the reference compounds to prepare the corresponding methyl substituted compound. One having ordinary skill in the art would have been motivated to prepare the instantly claimed compounds because

such structurally analogous compounds are expected to possess similar properties. It has been held that compounds that are structurally homologous to prior art compounds are *prima facie* obvious, absent a showing of unexpected results. *Ex parte Bluestone*, 135 USPQ 199, and *In re Doebel*, 179 USPQ 158 wherein it was affirmed that N-CH_3 is obvious over N-H.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3-9, 13 and 14 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7 and 9-15 of U.S. Patent No. 7,091,209. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and reference claims are drawn to structurally analogous compounds.

The reference claims are drawn to 2-aryldihydroxypyrimidine-4-carboxylic acid compounds useful as inhibitors of hepatitis C virus polymerase, see formula (I) in claim 1 and the corresponding species. The reference discloses that the compounds exist in equilibrium with the corresponding tautomeric form of structural formula (IA) as disclosed in col. 1. The instant claims differ from the reference compounds by having the substituent attached to the ring nitrogen atom, R^1 as an alkyl group, e.g., a methyl (CH_3), as compared to the reference compounds of formula (IA), which have H in the analogous position. Therefore, the instantly claimed compounds differ from the reference compounds by having H vs. CH_3 group and the structural similarity of compounds differing by a methyl in place of the hydrogen (i.e., H vs. Methyl) is well established. It would have been obvious to one having ordinary skill in the art at the time of the invention to modify the reference compounds to prepare the corresponding methyl substituted compound. One having ordinary skill in the art would have been motivated to prepare the instantly claimed compounds because such structurally analogous compounds are expected to possess similar properties.

Receipt is acknowledged of the Information Disclosure Statement filed on March 30, 2006 and a copy is enclosed herewith.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Monday-Friday from 8:00am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Deepak Rao
Primary Examiner
Art Unit 1624

January 17, 2007